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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,287	MONTGOMERY ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment and remarks filed on 12/16/2003 are acknowledged. Claims 1 and 32 have been amended. Claims 1- 42 are currently pending in this application. Rejection of claims 1- 42 under 112, second paragraph has been overcome by the applicant's amendment.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 1-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chou et al. (U.S. Patent 5,821,357) in view of Bauman et al. (U.S. Patent 5,180,824) of record.

The claims 1-42 are directed to methods of synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine, which are defined as:

(1) Claims 1-19 are directed to a method of synthesis of 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The synthesis includes the steps of first reacting the anionic form of 2-chloro-6-substituted purine with a protected 2-deoxy-2-fluoro-D-arabinofuranose, then reacting the product with an alkoxide to provide 2-chloro-6-alkoxy purine nucleoside and finally, reacting the 2-chloro-6-alkoxy purine nucleoside with ammonia to yield the 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine;

(2) Claims 20-37 are directed to a method of synthesis of 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The synthesis includes the steps of first reacting the anionic form of 2-chloro-6-amino purine with a protected 2-deoxy-2-fluoro-D-arabinofuranose, then reacting the product with ammonia to yield the 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine;

(3) Claims 38 and 39 are directed to a method of synthesis of 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The synthesis includes the steps of first reacting the anionic form of 2-chloro-6-amino purine with a protected 2-deoxy-2-fluoro-D-arabinofuranose, then reacting the product with alkali metal alkoxide to yield the 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine; and

(4) Claims 40-42 are directed to a method of synthesis of 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The synthesis includes the steps of first reacting the anionic form of 2-chloro-6-azido purine with a protected 2-deoxy-2-fluoro-D-arabinofuranose, then reacting the product with a reducing agent and finally, reacting the product with base to yield the 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine.

Additional claim limitations set forth in dependent claims include the 6-substituted group in purine is a halogen, anionic form is an alkali metal salt or organic amine salt such as DBU; 3- and 5- hydroxyls of the arabinofuranose is selected from the group consisting of acyl group, ether group, and combinations thereof; the group at C-1 is selected from the group consisting of halo, alkylsulfonyloxy, and arylsulfonyl groups,

coupling reaction solvent is selected from the group consisting of acetonitrile, dimethylformamide or dimethylacetamide, and sodium methoxide is used as base and an alcohol is used with the base.

Chou et al. teach the synthesis of 2'-deoxy-2'-fluoronucleosides wherein 2-deoxy-2-fluoro-3,5-di-O-benzoyl alpha-D-arabinosyl bromide is reacted with a metal cation salt or anionic form of a nucleobase (purine) (see col.2, lines 38-48 and col.10, lines 40-54).The preparation of 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-substituted nucleosides where 6-substituted purine is substituted with a halo, amino,or alkoxy group is disclosed in col. 7, lines 36-67 and col. 13, example 3. Chou et al. disclose the reaction of anionic form of a 2-halo-6-substituted purine in col. 5, lines 1-17.The cation salts which were used to convert a nucleobase into an anionic form are disclosed in col. 10, lines 40-54 and the organic amine cation salt DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) is disclosed in col. 9, line 1-2. In col. 2, line 67, the reaction solvents are disclosed, especially dimethyformamide or dimethylacetamide. Chou et al disclose in col. 8, line 45, the use of benzoyl group to produce a protected sugar for the glycosylation process. Also, Chou et al. disclose the removal of protecting groups by using ammonia or sodium methoxide in alochol, see col. 11, lines 39-43 and 45-48. While Chou et al. teach the synthesis of 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amino nucleoside from the intermediate 6- halo, amino, or alkoxy substituted purine nucleoside, Chou et al. differ from applicant's process in that Chou et al. do not suggest the use of 6-azido substituted purine nucleoside intermediate

in the synthesis of 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amino nucleosides.

Bauman et al. teach the use of 6-azido-2-fluoropurine intermediate in the synthesis of purine nucleosides (see abstract). Bauman et al. teach a method reducing the azide to an amine by hydrogenation over a palladium catalyst (reducing agent) in an alcoholic solvent to prepare the nucleoside 9-ß-D-arabinofuranosyl-2-fluoroadenine, see col. 4, lines 17-45 and claim 2. It is noted that Bauman et al. does not provide specific disclosures regarding the reduction of azido to an amine in the intermediate 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-azido nucleosides.

Therefore, one of ordinary skill in the art would have found the applicants claimed methods of synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine using the intermediate 6- halo, amino, azido or alkoxy substituted purine nucleoside, to have been obvious at the time the invention was made having the above cited references before him. Since Chou et al. teach the synthesis of 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amino nucleoside from the intermediate 6-halo, amino, or alkoxy substituted purine nucleoside and Bauman et al., teach reduction of azido to an amine in the intermediate 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-azido nucleoside, one skilled in the art would have a reasonable expectation for success in combining both references to accomplish a

method for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The motivation for doing so is provided by Chou et al., which suggests that the high yields of beta nucleosides could be obtained from 2-deoxy-2-fluoro-3,5-di-O-benzoyl-alpha-O-arabinosyl bromide via S_N2 displacement (see col. 2, lines 42-48).

Rejection Maintained

Rejection of claims 1-42 under 35 U.S.C. 103(a) is maintained for the reasons of record. Applicant's arguments traversing the rejection of claims 1-42 under 35 U.S.C. 103(a) have been fully considered but they are not persuasive.

Response to Arguments

Applicants argue, "Chou does not relate to 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. With respect to Claims 1-19 and 23, Chou fails to even remotely suggest a reaction of a purine nucleoside having a 6-alkoxy group to the desired final product". Chou teaches the preparation of 2'-deoxy-2',2'-difluoronucleosides and 2'-deoxy-2'-fluoronucleosides (col. 7, lines 36-67) wherein the purine moiety can be substituted independently with a halo group at C-2 and an amino group at C-6 (see col. 6, (VII)). It is noted that 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine is rendered obvious in view of the prior art which discloses the preparation of 2'-deoxy-2'-fluoronucleosides wherein the purine moiety is substituted with a halo group at C-2 and an amino group at C-6. Furthermore, Chou discloses the glycosylation process wherein the nucleobase purine is substituted with an alkoxy group at C-6 (col. 6, line 18).

Applicants also argue, "Bauman fails to overcome the above discussed deficiencies of Chou with respect to rendering obvious claims 1-42." Chou et al. differ from applicant's process in that Chou et al. do not suggest the use of 6-azido substituted purine nucleoside intermediate in the synthesis of 2-halo-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amino nucleosides. Bauman et al. teach the use of 6-azido-2-fluoropurine intermediate in the synthesis of purine nucleosides (see abstract).

Indeed, the examiner has established a prima facie case of obviousness rendering claims 1-42 rejected under 35 U.S.C. 103(a) by addressing sufficiently all of the limitations set forth in the instant methods of synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine, one skilled in the art would have a reasonable expectation for success in combining the teachings of Chou et al. and Bauman et al. references to accomplish the synthesis of synthesizing 2-chloro-9-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine. The motivation for doing so is provided by Chou et al., which suggests that the synthesis of 2-deoxynucleosides and their analogues is reflected in their use as therapeutic agents in viral and cancerous diseases (see col. 1, lines 19-22).

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
May 17,2004

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600